TRANSITION OF CARE FOR PULMONARY FIBROSIS PATIENTS

CANDIDATE FOR LUNG TRANSPLANT

An educational manual for patients and caregivers

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PREFACE

During my clinical practice in pulmonary fibrosis, I soon came to realize that the period of transition when a patient is referred for lung transplantation is very stressful for the individual, for the caregiver(s) and, quite frankly, for the physician too. Uncertainties about the possible qualification for transplant, timing for listing and actual transplant, and outcomes (with and sometimes without a transplant!) create a wide array of worries. Moreover, all this happens while we are dealing with an aggressive disease that often continues to get worse. The whole process resembles to a race where the respirologist, the transplant team, the patient and the caregiver(s) all try to keep that transplant window open.

I then thought that a practical manual to navigate a period of transition that is at the same time stressful and hopeful would be of some use. The manual is not meant to replace a full guide on lung transplantation provided by the Lung Transplant Programs, but is simply an integration of the existing educational material.

I would like to thank all contributors for their most useful inputs, and the patients for their…patience and resilience in the face of adversity!

Marco Mura, London, ON, November 2021

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I. Introduction to lung transplant for patients and caregivers (M. Mura)

Lung transplant (LTx) is a lifesaving procedure for subjects with serious respiratory illness, including emphysema and chronic obstructive pulmonary disease, interstitial lung disease (ILD) and pulmonary fibrosis (PF), pulmonary hypertension (PH) and cystic fibrosis.

LTx is a complex surgical procedure to replace 1 or 2 diseased lungs of the patient with healthy lungs from a compatible donor. The "new" lungs are then expected to work much better than the lungs affected by PF, immediately improving gas (oxygen and carbon oxide) exchange capacity and oxygenation for the recipient. After a LTx, most patients no longer need supplemental oxygen, and many return to a productive life. Pulmonary fibrosis never comes back to affect the transplanted lungs (also commonly known as "graft"). However, it is fundamental to understand that the patients undergoing a LTx exchange an old problem (PF in this case), with an all-new set of problems related to LTx and lifelong immunosuppression, leading to risks of infection and rejection.

For patients with interstitial lung disease (ILD) evolved to pulmonary fibrosis (PF), LTx is considered when progression of disease is observed, despite optimization of therapy with the available drugs. In any case, LTx is considered when the disease is approaching an advanced stage, or when is already advanced at the time of diagnosis. Indeed, LTx often represents the only chance for longer survival in patients with advancing PF, already on supplemental home oxygen therapy. This is due to the fact that PF equals to scarring in the lungs and is not reversible. Any additional progression of disease further reduces lung function and, as a result, quality and quantity of life.

Either 1 or 2 lungs can be transplanted. The single LTx operation is shorter and a better option for patients who have some cardiac (heart) issues, but there is a strong prevalence (80%) of double LTx in Toronto, as it provides a better long-term lung function. The LTx surgeon decides

which option is best for the individual patient, but both single and double LTx are proven to significantly improve survival in patients with advanced stage PF who are appropriate candidates.

II. The referral, assessment and listing process (M. Mura)

LTx in Ontario are done only at Toronto General Hospital, which is also the biggest centre in Canada, and also services the Maritime provinces. Remarkably, the first successful single and double LTx were done in Toronto in 1983 and 1986, respectively. Since then, the Toronto Lung Transplant Program has remained a world leader in LTx, with high volumes of transplants and ongoing, ground-breaking research. Other LTx centres in Canada are Montreal, Winnipeg, Edmonton and Vancouver.

It is important to understand that, when the PF disease is advanced, a LTx referral poses significant challenges, as the assessment process takes up to 6 months. If potential barriers to LTx are identified, such as coronary blockages in the heart, it can take even longer. During this process, further progression of PF can occur, not only putting the life of the patient in danger, but also making the subject potentially ineligible for the LTx itself. The general approach is then to refer patients quite early to ensure that the assessment is not rushed and the patient remains a candidate for LTx at the end of the assessment. For patients with rapidly deteriorating disease and who are otherwise deemed potentially good candidates for LTx, urgent referrals/assessments remain an option.

Tests done in preparation for the LTx assessment include:

- Chest CT scan (should not be older than 1 year)
- Echocardiogram (ultrasound of the heart)
- Lung perfusion scan (a nuclear medicine test to see if the blood goes more to the

right, or more to the left lung)

- Myocardial perfusion imaging (MIBI), otherwise known as a nuclear stress test (evaluates blood flow to the heart at rest and under stress)
- Bone mineral density scan
- Doppler ultrasound of arteries (to check for obstructions)
- Pulmonary function tests and 6-minute walk test - typically already available, as part of routine practice in clinic

While LTx takes place only in Toronto, the majority, if not all the tests required are done at the local, referring centre. Once the required tests are collected, the referral is sent and the patient is assessed by a LTx respirologist. The LTx respirologist will explain in detail to the patient and caregiver(s) the requirements and possible barriers to be listed for transplant. Barring any immediate contraindications, the actual assessment will then follow in Toronto.

A LTx assessment is not a guarantee for listing, as sometimes, unfortunately, some issues that make LTx not a viable option are discovered during the assessment process. We then always encourage patients to remain hopeful and do their best to be eligible for LTx, but also to have realistic expectations. There are no specific age limits for a LTx assessment in Toronto, but, as age advances, it progressively becomes more difficult to be listed.

A LTx assessment may be completed when the patient is still early to be listed. In this case, the option of LTx may be considered at a later time, when needed. A time window for LTx listing exists. Patients should be sick enough to benefit from LTx in terms of actual survival, but should also not be too sick and still be able to carry on an exercise program on a regular basis, even if they need a very high amount of oxygen. The reason for not listing or de-listing patients who are

very sick and not able to carry on any exercise activity for several weeks is that very poor LTx outcomes are always observed in these cases, making the LTx procedure a failure, rather than a success.

Keeping all this in mind, the expectations for the patient being considered for LTx are the following:

- undergo all required tests and take the prescribed medications;
- join and attend a supervised physiotherapy/exercise program on a regular basis - the referring centre will take care of arranging this;
- have supports in place from family or friends - this is required because progressing of disease can occur while on the waitlist, and the patient may not be able to drive him/herself to appointments;
- remain entirely smoke-free - this includes also vaping and smoking marijuana, which are not allowed.

When a patient is deemed eligible to be listed for LTx, the priority on the list is based on the severity of disease, and not on the time when the patient is listed. This is to ensure that rapidly deteriorating patients are transplanted sooner. Indeed, listing priority is a dynamic process that can change over time with the clinical condition of the patient. This is why the referring centre plays a fundamental role in following the patient and informing the transplant centre about any serious deterioration.

The website of the Toronto Lung Transplant Program is: https://www.uhn.ca/Transplant/Lung_Transplant_Program

The link to the Lung Transplant Manual for patients is: https://www.uhn.ca/Transplant/Lung_Transplant_Program/Documents/Living_Donor_Lung_Transplant_Manual.pdf

This a very useful read for patients and caregivers interested in LTx, written in lay language.

III. Management of medical therapy while LTx is being considered and while the patient is listed (M. Mura)

While a patient is considered for LTx, he/she is taken care of by the referring respirologist, unless the patient moves to the Toronto area. In that case, all medical care is taken over by the Toronto Lung Transplant program and local respirologists.

The continuation of therapies in patients with PF who are candidates for LTx is beneficial. PF is treated with either immunomodulatory (immunosuppressive) therapies (including prednisone, mycophenolate mofetil, azathioprine, methotrexate, cyclophosphamide, rituximab) or with anti-fibrotic therapies (pirfenidone, nintedanib). Occasionally, both types of therapy may be used in the same patient. In some other cases, such therapies are suspended, when they are deemed not helpful and causing side effects, no alternative therapies exist, and patients continue only with oxygen and palliative/symptomatic treatments.

Therefore, the referring respirologist's team at the local ILD clinic continues to manage and monitor the prescribed therapies, even when the patient is considered or listed for LTx. Given that most patients have advanced disease, a close follow-up is often required in this phase. As usual, patients and caregivers are encouraged to communicate with the coordinator at their local ILD clinic when they experience a worsening of their condition or new symptoms. The ILD

coordinator is a fundamental figure in keeping the physician appraised on the individual patient's clinical course, needs and concerns. Both the respirologist and coordinator pay particular attention to the identification of a patient's progression (worsening) of disease. This may trigger a more urgent LTx assessment, listing, or change of status on the LTx list, depending on the individual circumstances.

The issue of rapidly progressive disease in PF is discussed in detail in section VI. Once LTx takes place, most respiratory care is taken over by the Toronto Lung Transplant Program.

IV. Weight and nutrition optimization (S. Rinaldi, M. Mura)

A fundamental issue in pre-transplant care is weight optimization. A body mass index (BMI) between 17 and 30 is required for LTx. The BMI is calculated by dividing weight by the height squared. For example, for a subject with a weight of 80 kg and a height 1.75 m, the BMI is 80/(1.75x.1.75) = 800,000/30,625 = 26.

Unfortunately, weight is often a barrier to LTx listing, as research has shown a higher likelihood of poor outcomes after surgery when weight is too low, or, more often, too high. Ideally, BMI should be between 17 and 27 in order to receive a LTx, but up to 30 is still acceptable for LTx listing. A LTx assessment can be initiated at a BMI of 32, but a BMI of 30 needs to be reached before a patient can be listed for LTx.

When BMI is too low or high, or when a rapid change (either gain or loss) of weight is observed, a referral to a dietitian is very beneficial to help support with healthy weight optimization for LTx and improve overall nutritional health. Effective weight loss is often achieved with a regular exercise program, and can also help maintain muscle mass, even when oxygen requirements are high.

Weight loss or weight gain can be especially difficult when living with chronic lung disease due to a variety of factors such as medications side effects, difficulty breathing, fatigue, etc. As such, having a plan and surrounding yourself with the right supports plays an important role in weight optimization.

V. Physiotherapy and management of high flow supplemental oxygen therapy (M. Mura, L. Adams)

Physiotherapy is beneficial for patients with chronic lung disease, even if they do not qualify for a LTx. Attendance of a supervised physiotherapy program is a requirement for LTx listing. Many studies demonstrated that regular physiotherapy is associated with significantly improved outcomes of LTx. In other words, being in the best possible shape, despite a significant lung problem, will improve survival of patients undergoing LTx. Physiotherapy also increases the sense of control that the patient has over their disease. It has also been demonstrated that patients exercise much better when they are in a group, rather than on their own.

Patients are often quite anxious at the thought of exercising, when they have difficulty even doing their activities of daily living. However, working together with the physiotherapist, they are able to exercise safely and optimize their functioning, despite their lung condition.

Most patients being assessed for LTx will be on supplemental oxygen therapy, and some have been on it for a long time. Educating the patient about their oxygen needs is also a big part of the exercise program, given the large difference between “at rest” and “with activity”. We actually use an increased need for oxygen on exertion as a parameter to identify progression of disease.

A common problem in patients with PF is the underuse of supplemental oxygen during exertion, which leads to quite dramatic desaturations (drop of oxygen level) that can be dangerous to the heart, and greatly limit the subject with every activity. We use the 6-minute walk test to measure this, and supervised physiotherapy programs are also very helpful in identifying an increased oxygen requirement during exercise.

Another relatively common problem is the overuse of oxygen at rest, as some patients "feel better" when they use more oxygen, even when they do not strictly need a high flow at rest. Although not as common as in emphysema and COPD, overuse of oxygen at rest can lead to carbon dioxide retention, which can alter the mental status and be dangerous. When carbon dioxide retention occurs, the oxygen use is then corrected by the medical team and education is provided. Owning an oximeter, the little device to be put on the finger that tells you your oxygen saturation and heart rate, is very helpful to monitor oxygen needs, as long as an excessive use of the oximeter does not cause anxiety to the patient or caregiver.

By the time actual listing for LTx is approved, some patients may need a high amount of oxygen. In some other cases, oxygen requirements increase significantly while on the waitlist, but patients and caregivers should not be discouraged by this, as the flow of oxygen used per se does not affect the LTx outcome or LTx eligibility.

VI. Coordination of care with the Toronto Lung Transplant Program (M. Mura)

A fundamental issue in the medical care of patients with PF being considered and assessed for LTx is the detection of progression of disease, especially when this occurs in a rapid fashion, which is not uncommon.

Effective communication between treating respirologist and transplant respirologist is therefore very important. Patients are educated to contact the treating respirologist and/or the coordinator when their symptoms or oxygen requirements increase significantly, or rapidly. Even if the decision to list or not list lies with the Transplant Program only, the referring respirologist still plays an important role in providing information about the current patient's status.

As previously mentioned, transplant listing is a dynamic process, with different levels of priority that can change over time as the patient's condition evolves.

Communication with the pre-transplant coordinator in Toronto is also important to streamline the tests required to complete the LTx assessment, especially when extra-tests are required. Patients are then encouraged to contact their referring respirologist's office for any medical issue or concern, and also to contact the transplant coordinator in Toronto with questions in regard to assessment and listing. In any case, the referring respirologist's office will do their best to streamline the assessment process, so that a decision on listing can be reached sooner rather than later.

When patients are assessed early, they may not be sick enough to be listed, and regular follow-up with the referring respirologist continues. The decision to reconsider LTx when progression is observed is often shared by the patient and treating physician. If a long time has passed since the initial assessment, some tests may need to be updated.

At the other end of the disease range, rapidly progressive PF is a particularly challenging issue. A rapid worsening of this condition often leads to hospitalization, can put the life of patients in danger, and can even compromise their eligibility for LTx. For example, rapid deterioration of PF can involve areas of the lungs previously spared and functioning, leading to increased oxygen requirements and even need for mechanical ventilation in the intensive care unit (ICU). In this life-

threatening situation, the patient is put on hold on the LTx list, until he/she is better and able to rejoin the physiotherapy program, if reversible causes are present. Prolonged mechanical ventilation in PF is actually not recommended by ICU teams, given very poor outcomes, especially in older patients. This is why every effort is made to assess patients early and increase their status (priority) on the waitlist when rapid progression of disease is first observed. High-dose steroids for a short period of time may also be used to treat rapid progression of PF and improve the patient's status. The outcome of this therapy is remarkably unpredictable in PF, with some patients improving right away, and some others not improving at all. Another cause of rapid worsening is represented by pneumonia (infection) and this is usually associated with much better outcomes and recovery with the appropriate treatment.

VII. Depression, anxiety and how to deal with them (S. Yildiz)

Depression and anxiety are common among patients with PF and caregivers. Patients with PF may develop negative thoughts, feelings and emotions when the illness affects their daily functioning. These negative thoughts and feelings may cause loss of interest in activities, constant sadness, sleep disorders and fear for the future, with hopelessness. Professional help by a psychotherapist would improve the patients' life quality and give patients a sense of joy and meaningfulness in their lives. Through some therapeutic approaches, such as cognitive behavior and acceptance and commitment therapies, patients learn to be aware of their negative thoughts and feelings. Once they identify their negative thoughts and feelings, they learn a more helpful perspective to their illness through some interventions, including mindfulness with the "here and now" principle and behavioural experiments.

The role of Spiritual Care is emphasized. Integrating spirituality into psychotherapy would often yield better results. When patients are unable to make meaning in their physical problem through therapeutic interventions, it would be helpful to search for their spiritual resources. Individual patients may have different understandings of spirituality, depending on their culture or background. Based on personal spiritual resources, spirituality helps patients make meaning about their illness, gain strength and hope through their faith practices.

VIII. Management of symptoms and the role of palliative care (S. Malik, M. Mura)

The role of palliative care is increasingly recognized in PF even in patients who are considered and even actively listed for LTx.

Palliative care is most commonly introduced late in the course of PF and other diseases, when the patient's main healthcare team is concerned that their current therapies are ineffective and there may only be weeks to months of life left. However, there is growing recognition that earlier referral to palliative care is better. For patients with advanced lung diseases such as PF, adding an extra-layer of supportive or palliative care to their existing health care services can lead to decreased depression, anxiety and improved management of symptoms and quality of life. In PF, the main symptoms are represented by shortness of breath, cough and fatigue. This evidence has led to the creation of specialist palliative care teams, who are involved in the care of patients with PF. Some patients with complex needs who are eligible for LTx may be seen by a palliative care team as well.

The principles of palliative care assessment are similar to those of pulmonary rehabilitation. Patients and their families can expect a comprehensive assessment of their unique physical, emotional and social health care needs. Additionally, palliative care assessments include

conversations aimed at clarifying a patient's values and priorities for health. Given the uncertainty and complexity of care faced by many patients with PF, these conversations evolve over time. Working with other specialists to ensure that a patient's health care is aligned with their values is a key part of palliative care teams' role. Palliative care teams typically consist of nurse and physician specialists and may include psychologists, social workers, and spiritual care providers. Community palliative care teams exist throughout Ontario. These community teams offer home-based consultation and work closely with family physicians and specialists.

IX. Frequently asked questions (M. Mura, T. Brady, S. Yildiz)

Q: How long does it take after assessment until you are advised if you are going to be on the list?

R: It takes 2-4 weeks.

Q: There is a great deal of stress and anxiety while waiting for the answer. How do we deal with that?

R: It is very normal and natural to have stress and anxiety while waiting for the answer, because it is your health and it is affecting your daily functioning and future. Such stress may cause painful thoughts and feelings about many things, including yourself and your future. Primarily, it is important to acknowledge these thoughts and feelings instead of fighting, oppressing, or denying them. Cognitive defusion and mindfulness techniques that you can learn from professionals (psychotherapists, psychologists) help you focus on the present moment and practice self-compassion and self-care. It is also important to evaluate this waiting period by enhancing your strength through your social and spiritual resources.

Q: Are there any additional tests required after assessment and before listing?

R: The heart catheterization, also commonly known as “angiogram”, is the test done to check blockages in the coronaries. It is a very important test to determine eligibility for transplant. Since heart catheterization is an invasive test, in non-urgent cases it is the last test done, before a decision is made about listing.

Q If a person is listed, who determines the Lung Allocation Score (LAS).

R: The Toronto Lung Transplant Program determines the LAS.

Q: Will I get a single or double transplant?

R: A double (bilateral) lung transplant is done much more often, but single transplant is a shorter operation and it is deemed safer for some selected patients. The on-call transplant surgeon takes the final decision on single vs. double lung transplant, but there are patients who can only receive a double transplant (for example, due to the presence of pulmonary hypertension - high pressure inside the lungs).

Q: After I go home, can I have my follow-up with the local hospital?

R: No, most of the follow-up is done at Toronto General Hospital, given their unique expertise on lung transplant, especially during the first year post-transplant. However, pulmonary function tests and bloodwork can be done locally.

Q: Am I too old for a transplant? What facts determine eligibility?

R: The Toronto Transplant program currently does not have a specific age limit, and so even people over age 70 can potentially be considered. As age advances, it gets progressively more difficult to be eligible, given other possible health problems and lack of physiotherapy capability.

Q: What is the situation concerning smoking, e-cigarettes, or any other nicotine replacement product?

R: There isn't any form of smoking or vaping allowed, as they would damage the new lungs. To be eligible for listing, the patient needs to be smoke-free, vaping-free and smoked marijuana-free (edibles are accepted) for at least 6 months.

Q: Does one have to be in excellent health except for the lungs to be considered for transplant?

R: One needs to be otherwise in good health. Minor problems in other organs may not represent a barrier to listing for transplant.

Q: Caregivers generally feel that they are required to place the patient's needs ahead of their own. Unless you place yourself first, you will not be able to give your all when helping your loved one.

R: The well-being of caregivers is vitally important. When caregivers put their own needs aside because of feeling guilty or selfish, they eventually get so overwhelmed that they may not find time and energy to take care of their loved ones. Caregivers need to take care of themselves not only for their own sake, but also to be able to provide better help for their loved ones.

- It is essential for caregivers to apply care and compassion also for themselves.

- For this, first, they need to watch for signs of burnout such as chronic fatigue, loss of appetite, difficulty in falling asleep, loss of interest.
- Taking time for themselves will help caregivers reload their energy for the care they give to their patients.
- Asking for help from others when necessary will make the caregivers feel that they are not alone in their struggle.
- Doing exercise and/or meditation will not only help physically and mentally, but also will allow them to reflect on the care they give that it is meaningful and does make a change.

Q: Should there be some type of communication system in place so that one can check on how the patient is feeling and pass on the info to the transplant team, if necessary?

R: Absolutely. The coordinator in the ILD clinic and the physiotherapist following the patient both keep the treating respirologist aware of changes with the patient. Follow-up in the ILD clinic is also quite frequent at this stage. Communication between the treating respirologist and the Transplant team then plays a fundamental role in prioritizing patients on the waitlist.

X. General advices during the transition (T. Brady)

• Plan your journey. Get your rest, exercise and proper food to be in the best shape physically and mentally.

• Keep track of medical information and instructions (health professionals, medications, appointments, and medical milestones).

• Use the oximeter to monitor the oxygen saturation at rest and especially during exertion, but without continuously checking it. A progressive increase of oxygen requirements is usually expected.

• Communicate new concerns to the ILD coordinator in the clinic where you are followed.

• Maintain realistic expectations. given the unpredictable nature of some aspects of transplant. Hope for the best, and prepare for the worst.

• Caregivers: do not be afraid to ask for help when times get tough. Think about who you can depend upon when you become overwhelmed (friends, faith group, or support group)

• Link to the list and contact information of **Pulmonary Fibrosis Support Groups** in Canada: https://cpff.ca/community/support-meetings/

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